Systolic inter-arm blood pressure difference is associated with increased cardiovascular and all-cause mortality

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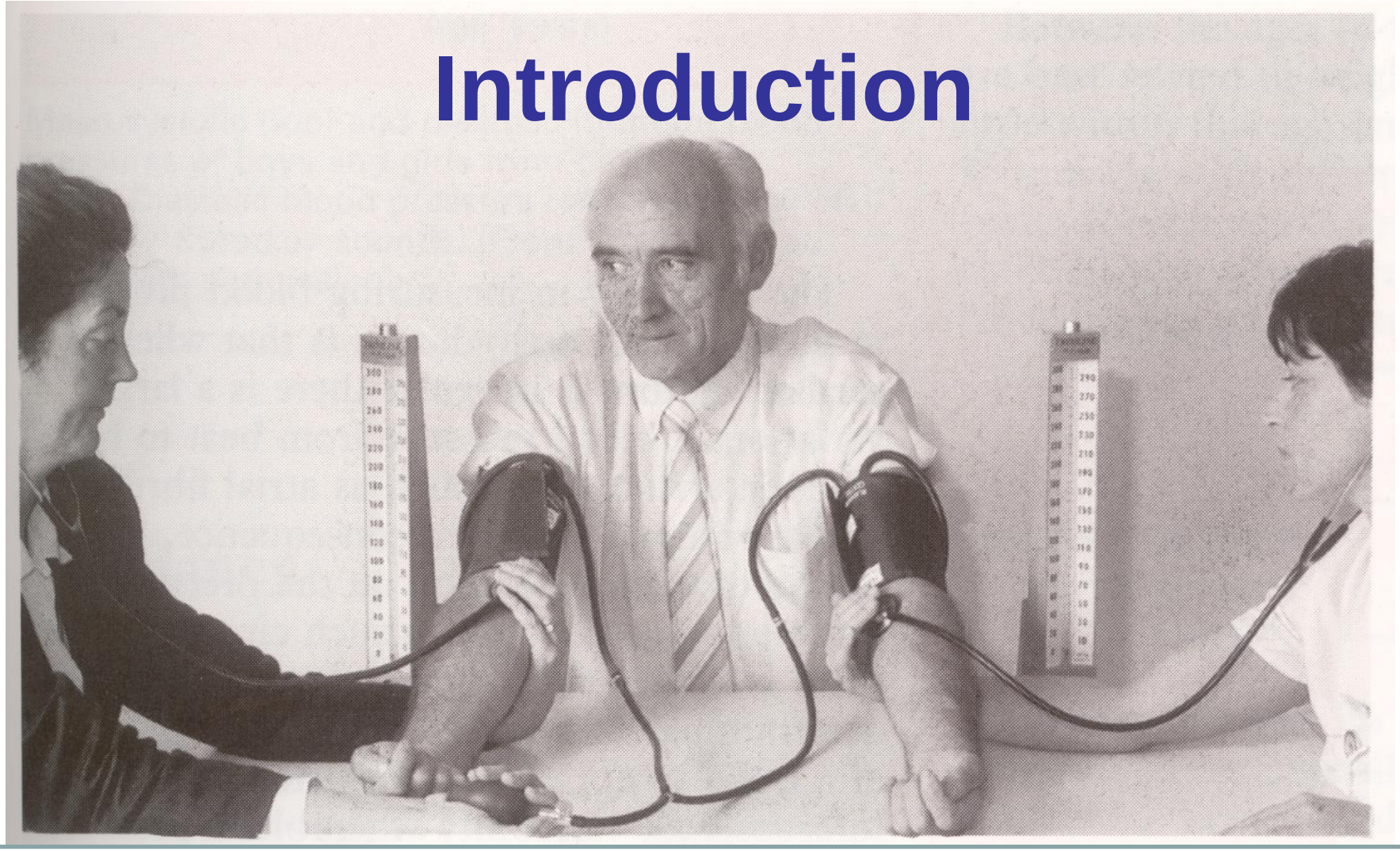
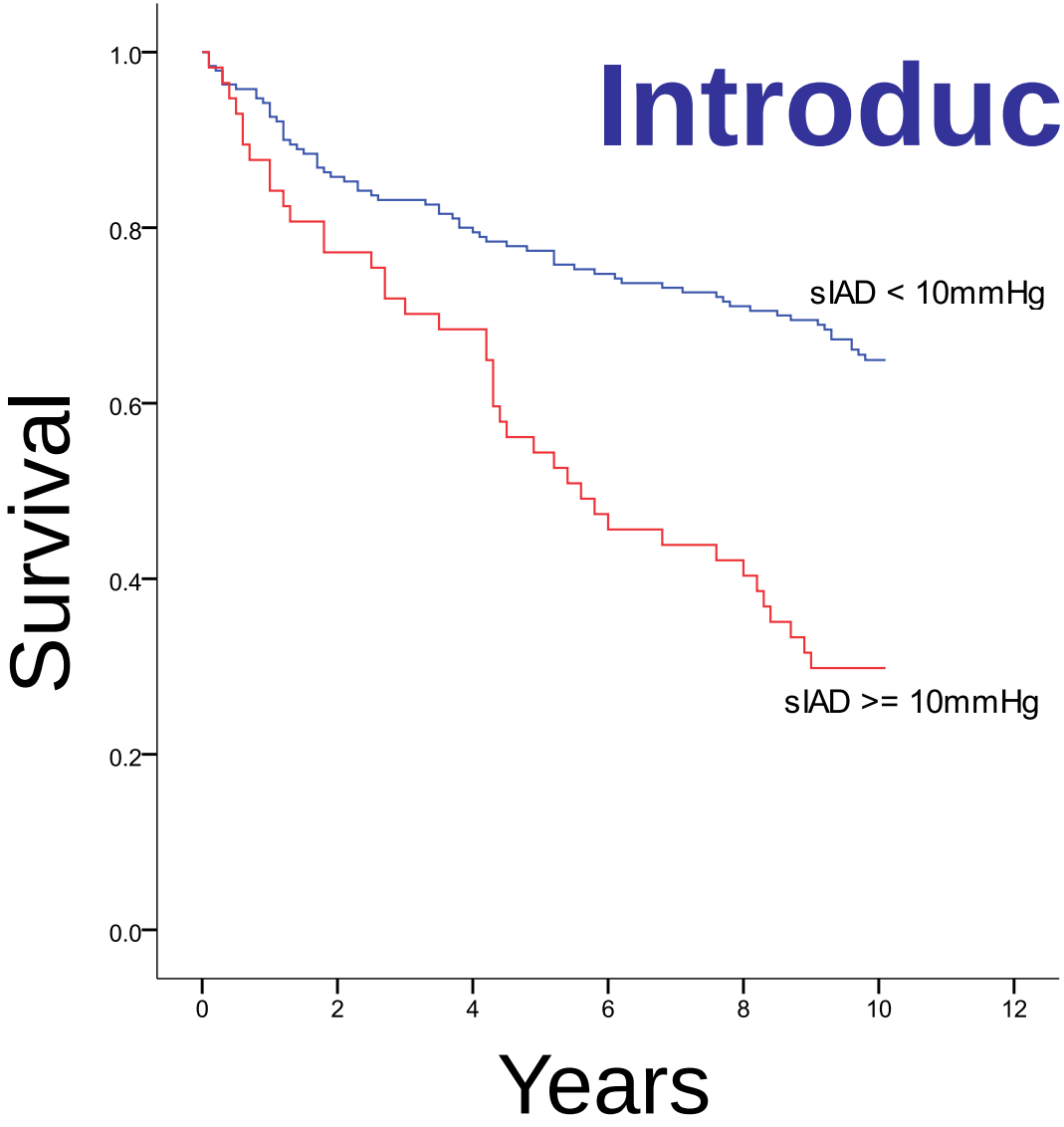
Introduction



O'Brien, E, Beevers D.G. & Marshall, H.J. 1995. ***ABC of hypertension***, 3rd ed. London, BMJ Publishing Group.

Introduction



All cause mortality for 247 subjects over 10 year follow up

10mmHg cut off

HR 3.4 [1.8 to 6.2]; p<0.001

The Mid Devon Medical Practice

Introduction

- Inter-arm difference is common
- Association with peripheral vascular disease
- Association with increased mortality in cohorts at high vascular risk

Rationale for further studies

- Such subjects are likely to have all risk factors managed anyway
- Existing evidence derived from cohorts at elevated vascular risk
- Can these findings be generalised to the a general population relevant to primary care?

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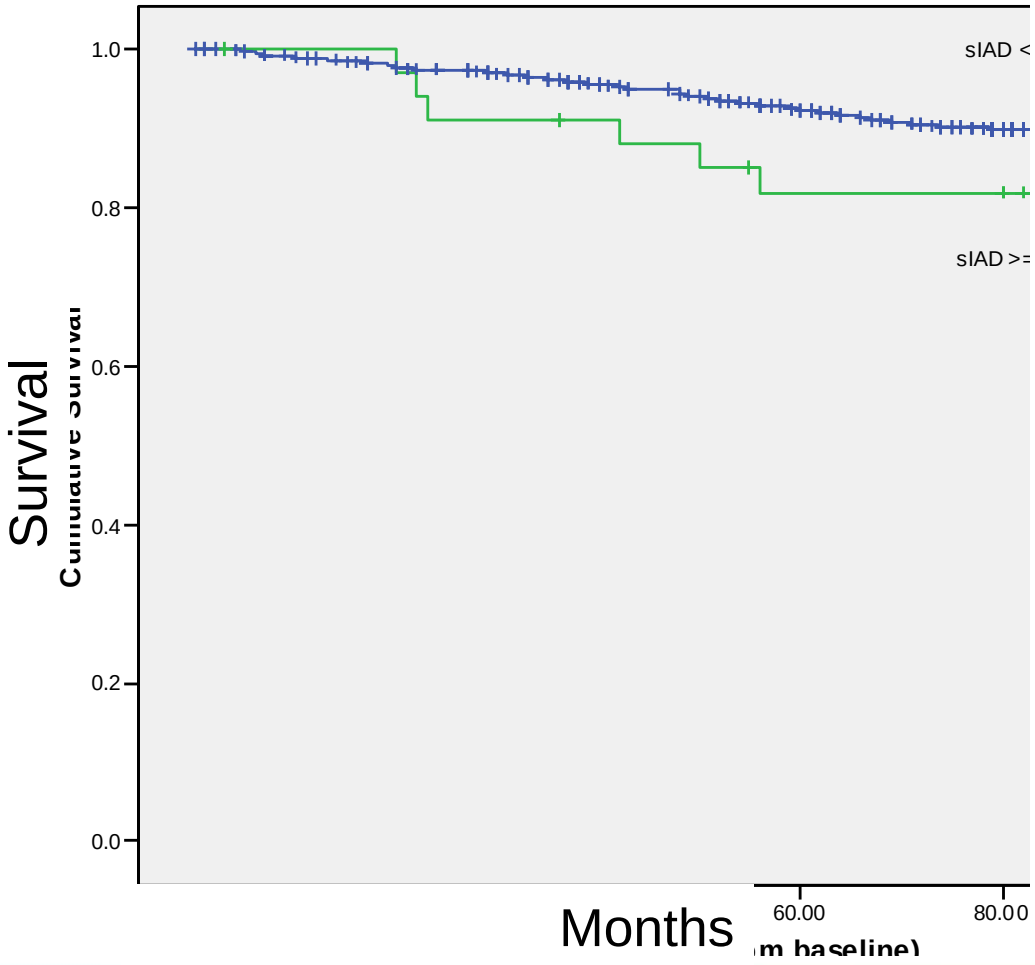

All cause mortality for 1316 subjects over 6 year follow up

15mmHg cut off

HR = 1.4 [0.7 to 2.6]; NS

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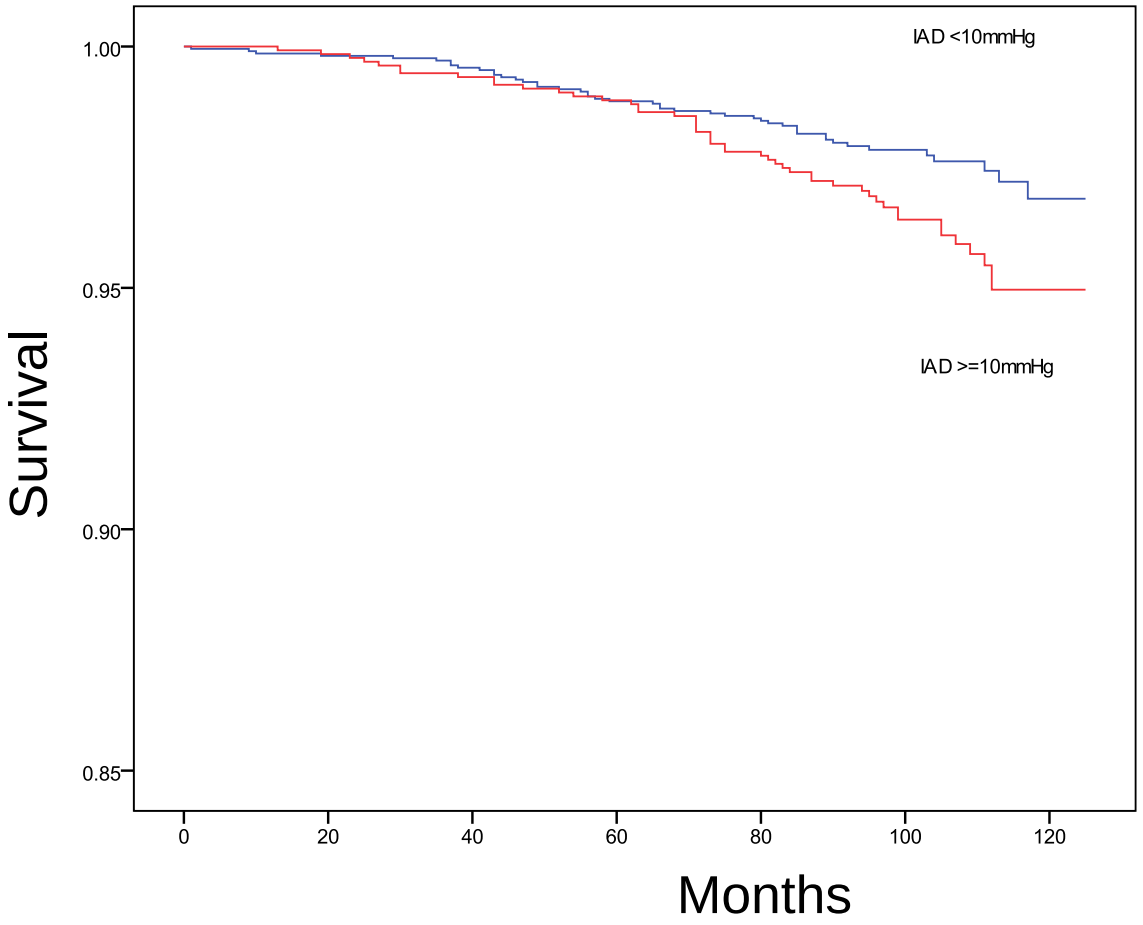
Aspirin in Asymptomatic Atherosclerosis trial (AAA)



Cardiovascular mortality plot for 3350 subjects over 10 year follow up

10mmHg cut off

HR = 1.5 [1.0 to 2.3]; p<0.05

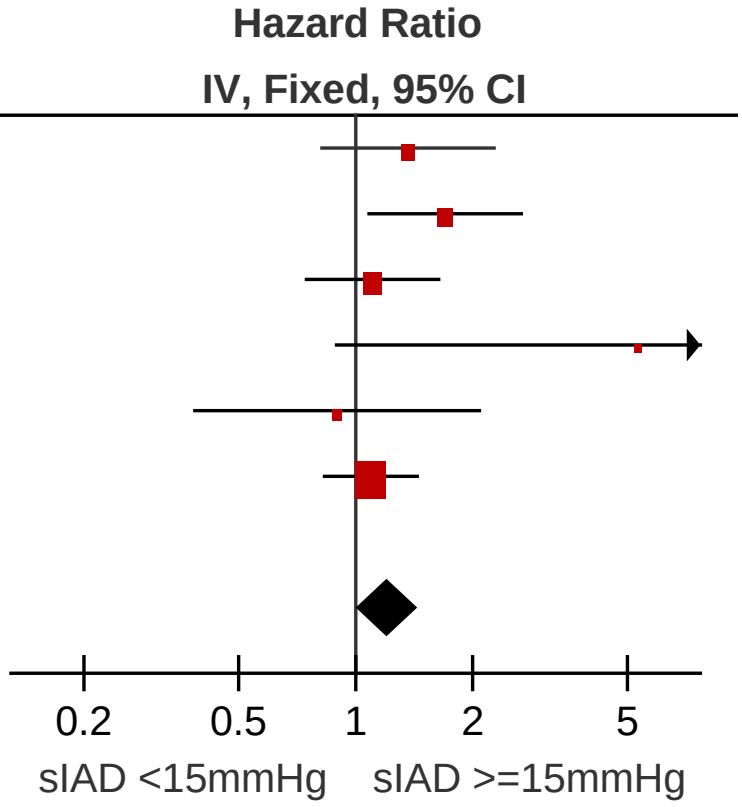
Results: all subjects

All cause mortality with 15mmHg systolic inter-arm difference

Study or Subgroup	Hazard Ratio IV, Fixed, 95% CI
Aboyans 2007 (1)	1.36 [0.82, 2.27]
Aboyans 2007 (2)	1.70 [1.08, 2.67]
Aboyans 2007 (3)	1.11 [0.75, 1.64]
Clark 2002	5.31 [0.89, 31.61]
Ferrucci 2000	0.90 [0.39, 2.08]
Fowkes 2010	1.09 [0.83, 1.44]
Total (95% CI)	**1.22 [1.02, 1.46]**

p <0.05

Total 1485 events; 6527 subjects



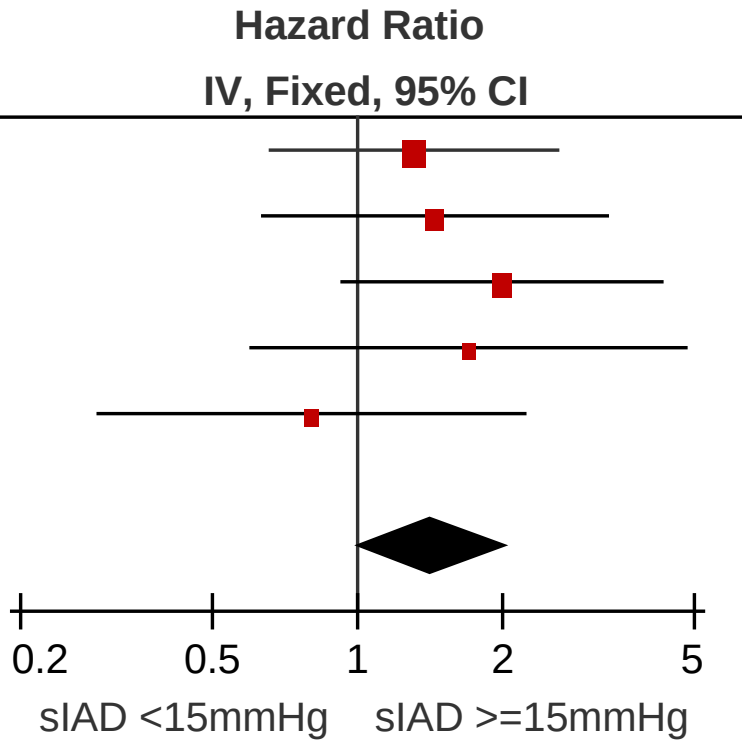
Results: all subjects

Cardiovascular mortality with 15mmHg systolic inter-arm difference

Study or Subgroup	Hazard Ratio IV, Fixed, 95% CI
Aboyans 2007 (1)	1.31 [0.66, 2.60]
Aboyans 2007 (2)	1.45 [0.64, 3.30]
Aboyans 2007 (3)	1.99 [0.93, 4.28]
Ferrucci 2000	1.70 [0.60, 4.80]
Fowkes 2010	0.80 [0.29, 2.22]
Total (95% CI)	**1.43 [0.99, 2.08]**

P=0.06

Total 523 events; 6444 subjects



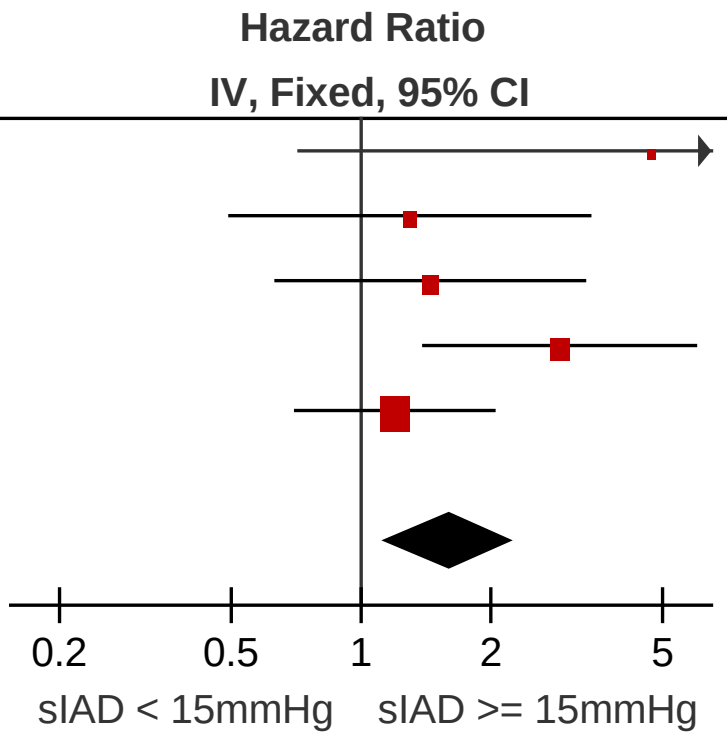
Results: hypertensive subjects

All cause mortality with 15mmHg systolic inter-arm difference

Study or Subgroup	Hazard Ratio IV, Fixed, 95% CI
Clark 2002	4.71 [0.72, 30.93]
Ferrucci 2000	1.30 [0.50, 3.39]
Aboyans 2007	1.45 [0.64, 3.30]
Clark 2007	2.89 [1.40, 5.96]
Fowkes 2010	1.20 [0.71, 2.03]
Total (95% CI)	**1.60 [1.13, 2.27]**

p =0.008

Total 456 events; 2231 subjects



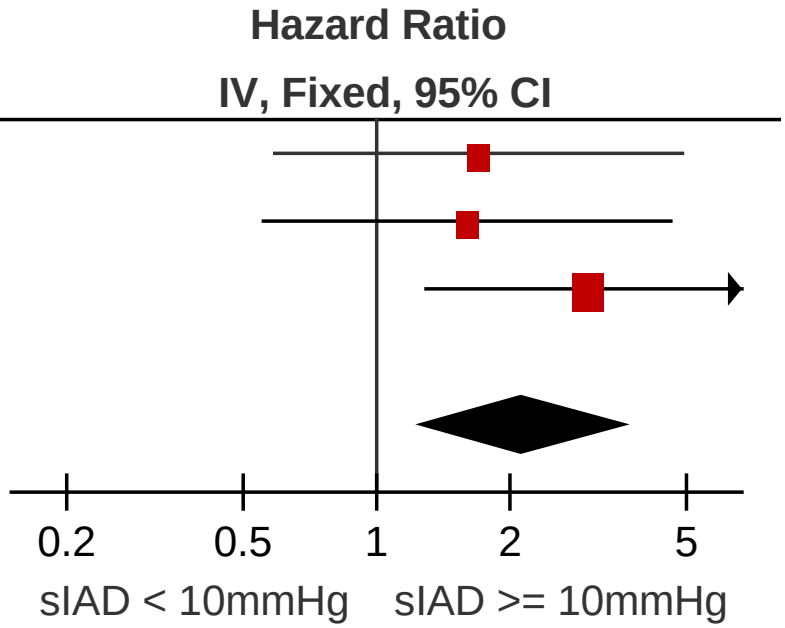
Results: hypertensive subjects

Cardiovascular mortality in hypertensive subjects with 10mmHg systolic inter-arm difference

Study or Subgroup	Hazard Ratio IV, Fixed, 95% CI
Ferrucci 2000	1.70 [0.59, 4.90]
Clark 2007	1.60 [0.56, 4.61]
Fowkes 2010	3.00 [1.29, 6.98]
Total (95% CI)	**2.15 [1.23, 3.76]**

P<0.01

Total 151 events; 1516 subjects



Conclusions

- An inter-arm difference ≥10mmHg or ≥15mmHg is associated with reduced survival in populations relevant to primary care

- Inter-arm difference should be looked for and aggressively managed when confirmed

Acknowledgements

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RCGP Royal College of General Practitioners

Scientific Foundation Board

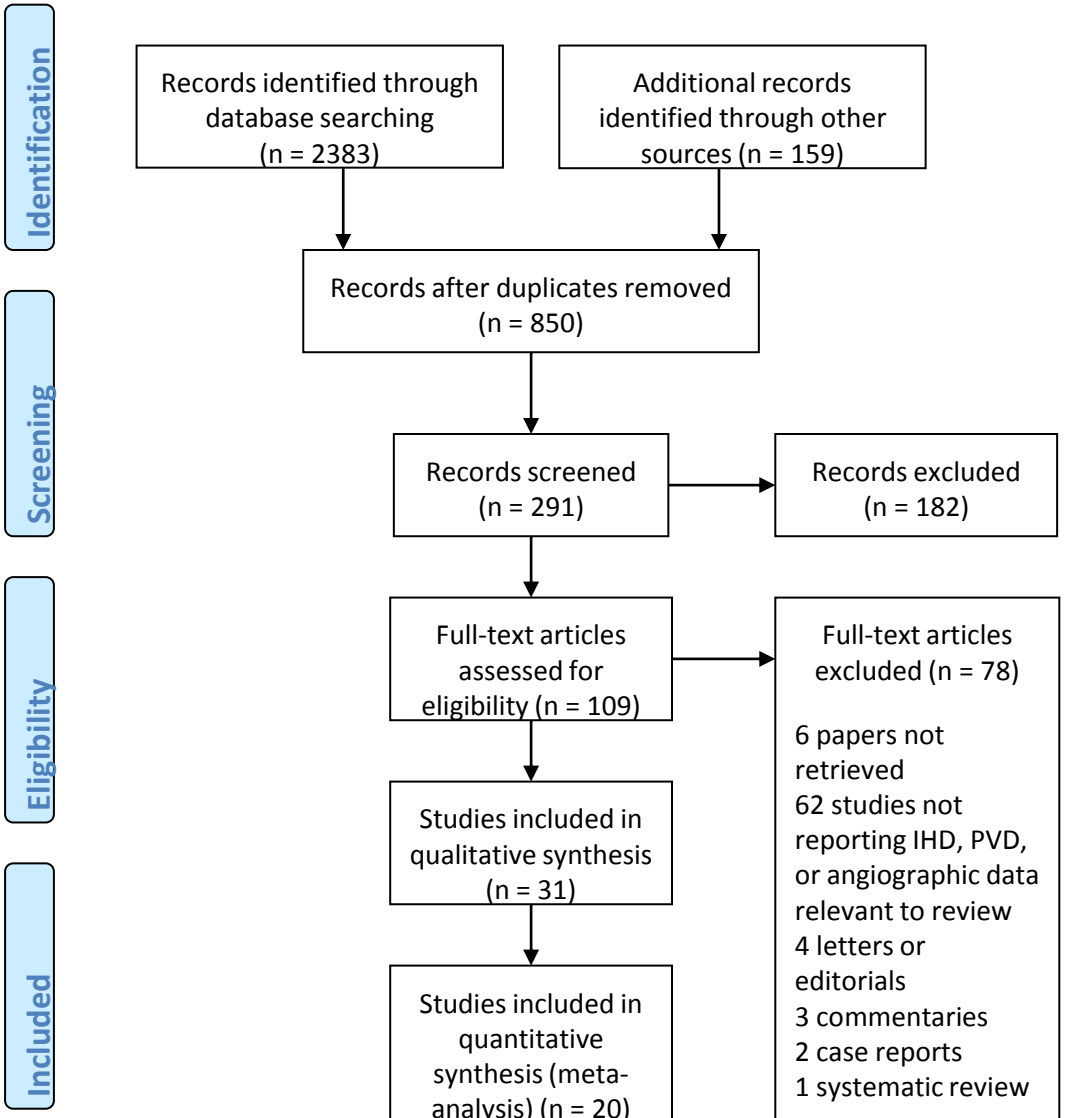
NHS National Institute for Health Research

Peninsula CLAHRC

Peninsula Medical School
Universities of Exeter & Plymouth

Supplementary slides

PRISMA flow chart for review:



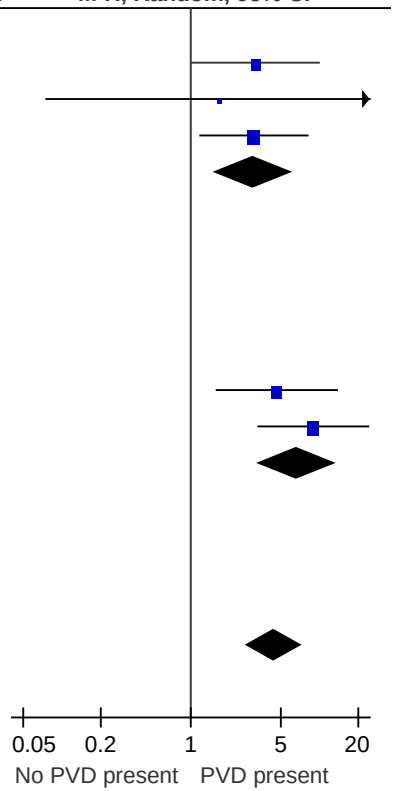
Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009; 339:b2535.

Cross sectional analyses

Prevalence of peripheral vascular disease with and without inter-arm difference ≥10mmHg

OR 4.46 [2.68, 7.41]
RR 2.44 [1.53, 3.87]

Study or Subgroup	sIAD >= 10mmHg Events	Total	sIAD < 10mmHg Events	Total	Odds Ratio M-H, Random, 95% CI
6.1.1 Simultaneous measurement technique					
Clark 2007	7	18	12	72	3.18 [1.03, 9.87]
Clark 2009	0	10	2	90	1.69 [0.08, 37.53]
Clark 2010	6	43	23	462	3.10 [1.19, 8.08]
Subtotal (95% CI)		**71**		**624**	**3.03 [1.49, 6.18]**
Total events	13		37		
Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 2 (P = 0.93); I² = 0%					
Test for overall effect: Z = 3.05 (P = 0.002)					
6.1.2 Non simultaneous measurement technique					
Frank 1991	24	29	34	67	4.66 [1.59, 13.66]
Kawamura 2008	13	20	39	227	8.95 [3.36, 23.89]
Subtotal (95% CI)		**49**		**294**	**6.65 [3.22, 13.74]**
Total events	37		73		
Heterogeneity: Tau² = 0.00; Chi² = 0.79, df = 1 (P = 0.37); I² = 0%					
Test for overall effect: Z = 5.12 (P < 0.00001)					
Total (95% CI)		**120**		**918**	**4.46 [2.68, 7.41]**
Total events	50		110		
Heterogeneity: Tau² = 0.00; Chi² = 3.22, df = 4 (P = 0.52); I² = 0%					
Test for overall effect: Z = 5.77 (P < 0.00001)					
Test for subgroup differences: Chi² = 2.30, df = 1 (P = 0.13), I² = 56.5%					



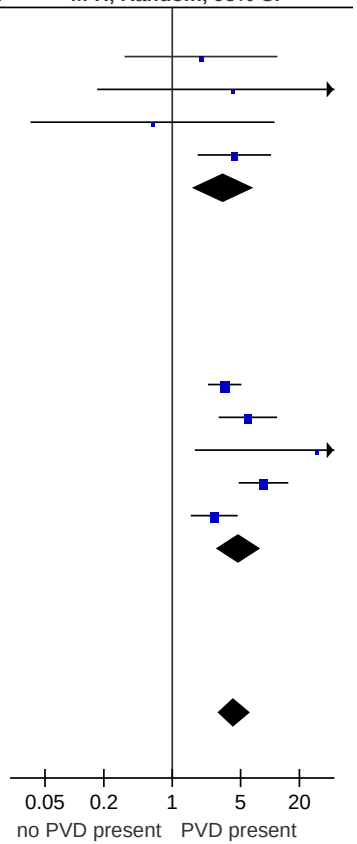
Cross sectional analyses

Prevalence of peripheral vascular disease with and without inter-arm difference ≥15mmHg

OR 4.32 [2.90, 6.43]
RR 2.48 [1.63, 3.77]

Study or Subgroup	sIAD >= 15mmHg Events	Total	sIAD < 15mmHg Events	Total	Odds Ratio M-H, Random, 95% CI
6.2.1 Simultaneous measurement technique					
Clark 2007	2	6	17	84	1.97 [0.33, 11.67]
Clark 2009	0	4	2	96	4.20 [0.17, 101.02]
Clark 2010	0	12	29	493	0.63 [0.04, 10.90]
Igarashi 2007	10	27	43	359	4.32 [1.86, 10.05]
Subtotal (95% CI)		**49**		**1032**	**3.36 [1.64, 6.89]**
Total events	12		91		
Heterogeneity: Tau² = 0.00; Chi² = 2.11, df = 3 (P = 0.55); I² = 0%					
Test for overall effect: Z = 3.31 (P = 0.0009)					
6.2.2 Non simultaneous measurement technique					
Aboyans 2010	35	307	232	6436	3.44 [2.36, 5.01]
Baribeau 2002	36	53	46	175	5.94 [3.05, 11.58]
Frank 1991	16	16	42	80	29.89 [1.73, 515.30]
Shadman 2004 (1)	21	55	190	2830	8.58 [4.88, 15.08]
Shadman 2004 (2)	69	87	670	1140	2.69 [1.58, 4.58]
Subtotal (95% CI)		**518**		**10661**	**4.80 [2.89, 7.99]**
Total events	177		1180		
Heterogeneity: Tau² = 0.20; Chi² = 12.83, df = 4 (P = 0.01); I² = 69%					
Test for overall effect: Z = 6.05 (P < 0.00001)					
Total (95% CI)		**567**		**11693**	**4.32 [2.90, 6.43]**
Total events	189		1271		
Heterogeneity: Tau² = 0.14; Chi² = 15.28, df = 8 (P = 0.05); I² = 48%					
Test for overall effect: Z = 7.20 (P < 0.00001)					
Test for subgroup differences: Chi² = 0.63, df = 1 (P = 0.43), I² = 0%					

(1) population cohort
(2) clinical cohort



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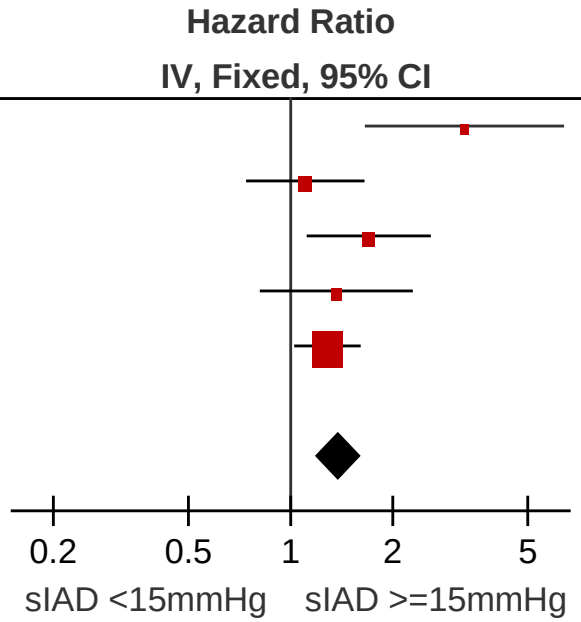
Results: prospective studies

All cause mortality with systolic 15mmHg inter-arm difference

Study or Subgroup	log[Hazard Ratio]	SE	Hazard Ratio IV, Fixed, 95% CI	Year
Clark 2007	1.18	0.34	3.25 [1.67, 6.34]	2007
Aboyans 2007 (1)	0.1	0.2	1.11 [0.75, 1.64]	2007
Aboyans 2007 (2)	0.53	0.21	1.70 [1.13, 2.56]	2007
Aboyans 2007 (3)	0.31	0.26	1.36 [0.82, 2.27]	2007
Agarwal 2008	0.25	0.11	1.28 [1.04, 1.59]	2008
Total (95% CI)			**1.38 [1.18, 1.62]**	

Heterogeneity: $Chi^2 = 9.01$, $df = 4$ ($P = 0.06$); $I^2 = 56\%$

Test for overall effect: $Z = 4.03$ ($P < 0.0001$)



(1) Cohort C

(2) Cohort B

(3) Cohort A

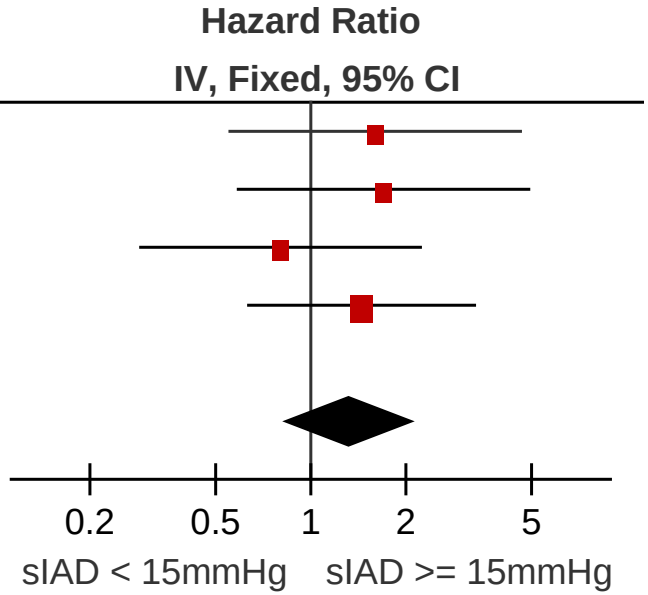
Results: hypertensive subjects

Cardiovascular mortality in hypertensive subjects with 15mmHg systolic inter-arm difference

Study or Subgroup	log[Hazard Ratio]	SE	Hazard Ratio IV, Fixed, 95% CI
Clark 2007	0.47	0.54	1.60 [0.56, 4.61]
Ferrucci 2000	0.53	0.54	1.70 [0.59, 4.90]
Fowkes 2010	-0.22	0.52	0.80 [0.29, 2.22]
Aboyans 2007 (1)	0.37	0.42	1.45 [0.64, 3.30]
Total (95% CI)			**1.34 [0.82, 2.18]**

Heterogeneity: $Chi^2 = 1.31$, df = 3 (P = 0.73); $I^2 = 0\%$

Test for overall effect: Z = 1.17 (P = 0.24)



(1) Cohort B: 82% with hypertension